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### Reply from the authors

We welcome the letter from Dr. Ureña Torres as it offers us an opportunity to clarify and emphasize several aspects of our measurements of the different bone alkaline phosphatase (BALP) isoforms in patients with chronic renal failure (CRF) [1]. In reply to his queries regarding questions 1 and 2, total ALP was significantly increased; however, the majority of the patients had activities within the reference interval for healthy adults. We agree with the suggestion that the increase of BALP isoform B2 in CRF patients may be clinically useful. None of the patients in this study had any biochemical or clinical evidence of hepatic disorder. To answer the third question, we used the previously reported reference intervals for all three BALP immunoassay kits (Alkphase-B, Tandem-R Ostase and Tandem-MP Ostase) and refer him to Figure 2 [1]. To respond to his fourth question, discordant findings between different studies are not uncommon, which probably reflects the heterogeneity of bone disorders in CRF patients. We did, however, find a significant correlation between the novel BALP isoform B1x and PTH, which might contribute to the positive correlations previously reported [2].

We suggested that B1x should be further evaluated as a marker of adynamic bone disease. This will indeed require a classification of patients by bone histomorphometry, which was not obtained in this study. Although adynamic bone disease is usually associated with relatively low parathyroid hormone (PTH) levels, PTH may fail to discriminate between adynamic and moderate hyperparathyroid states and even high PTH levels may occur [3]. Another important point, discussed in our paper [1], is that PTH was analyzed using a commercial assay originally reported to detect only the intact (1-84 PTH) circulating molecule. However, it has recently been demonstrated that a fragment (most likely the 7-84 PTH) interferes with this assay [4]. Thus, the PTH values reported in our study (and other studies) might well be higher than the true circulating levels of intact 1-84 PTH. Bone mineral density was not assessed and we prefer not to speculate as to whether these patients were osteopenic or osteoporotic.

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# Prediction of hypertension in hemodialysis patients

**To the Editor:** I have read with much interest the paper by Agarwal and Lewis [1] on prediction of hypertension in chronic hemodialysis patients. In the introduction, the authors focus on the fact that it is still uncertain which blood pressure measurement the clinician has to adopt to define hypertension in these patients. There is no question that in the general population 24-hour ambulatory monitoring is a better measure than the office measure. It is well-documented that the ambulatory estimate is superior to the office estimate for predicting incident cardiovascular complications, as well as left ventrical hypertrophy (LVH) [2], which is a valid surrogate end point. Whether or not 24-hour ambulatory monitoring predicts survival and cardiovascular complications in the dialysis population still remains to be proved. This is important mostly because two surveys have shown that routine pre-dialysis blood pressure and 24-hour ambulatory monitoring explain to a similar degree the variance in left ventricular mass. Both the paper by Conlon et al [3] and our study based on multivariate modelling [4] have clearly shown the strength of the association between 24-hour ambulatory monitoring and left ventrical mass is not superior to that of pre-dialysis blood

pressure (the average monthly value). Thus the idea of establishing the value of different blood pressure estimates (pre- and post-dialysis) assuming 24-hour ambulatory monitoring as a "gold standard" is unsupported because there is presently no proof that this estimate is a better predictor of cardiovascular outcomes in the dialysis population. We believe that 24-hour ambulatory monitoring is a valuable technique that may be usefully applied to the complex blood pressure alterations of end-stage renal disease (ESRD) patients. The blood pressure level that should be targeted for intervention is the level that determines the extent of vascular damage associated with hypertension. Because there is no solid evidence that 24-hour ambulatory monitoring is superioe to repeated pre-dialysis measurements (the average monthly value), we feel that it is of little use considering 24-hour ambulatory monitoring as the "gold standard" for the definition of hypertension in the dialysis population.

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### Reply from the author

Hypertension in dialysis patients has been mired in controversy with regard to outcomes [1, 2]. In fact, until quite recently, hypertension in hemodialysis patients was not even considered as a significant risk factor for cardiovascular morbidity and mortality [1, 3]. In contrast, studies done in patients with essential hypertension demonstrated a strong relationship between hypertension and survival even when blood pressure was in the high normal range [4].

Zoccali et al examined ambulatory blood pressure in addition to several other predictors in a cross-sectional study of 64 non-diabetic dialysis patients [5]. They did not study the 44-hour interdialytic blood pressure period but performed a single 24-hour blood pressure monitoring on a non-dialysis day. Unlike studies done in essential hypertension where office blood pressures are taken at one or two visits, the comparator blood pressure values were averaged for a whole month. After finding at least seven significant predictors of left ventricular mass that included dialysis unit blood pressure, they found that ambulatory blood pressure could not add precision to the multivariate prediction of the left ventricular mass. Therefore, in the context of model overfitting and multicollinearity, it should come as no surprise that the average pre dialysis blood pressure value over a 1-month period was as good (or as bad) at predicting the variance in left ventricular mass index. Similarly, a limited study of 35 patients cannot reject the hypothesis that ambulatory blood pressure is a better predictor of left ventricular mass compared to predialysis blood pressure [6].

We have demonstrated that a 2-week averaged dialysis unit blood pressure, either pre-dialysis or post-dialysis, can provide a reliable guide to the presence of hypertension or its control, but cannot accurately predict the level of blood pressure in dialysis patients [7]. Unlike dialysis unit blood pressure, ambulatory blood pressure monitoring is reproducible in this population; accordingly, fewer number of patients will be required to achieve similar power when using ambulatory blood pressure monitoring [8]. Based upon the above evidence, we speculate that once reliable estimates of blood pressure, such as with ambulatory blood pressure monitoring, are obtained, it will be easier to demonstrate the cardiovascular damage incurred by uncontrolled hypertension. Hence, until such studies are performed, ambulatory blood pressure monitoring must remain the "gold standard" for assessing the level of blood pressure in hemodialysis patients as in non-dialysis populations.

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